

## SEQUENCE LISTING

<110> De Francesco, Raffaele  
Tomei, Licia  
Behrens, Sven-Erik

<120> METHOD FOR REPRODUCING IN VITRO THE  
RNA-DEPENDENT RNA POLYMERASE AND TERMINAL NUCLEOTIDYL  
TRANSFERASE ACTIVITIES ENCODED BY HEPATITIS C VIRUS (HCV)

<130> IT0002PCA

<150> 08/952,981

<151> 1998-03-23

<150> PCT/IT96/00106

<151> 1996-05-24

<150> RM95A000343

<151> 1995-05-25

<160> 14

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Hepatitis C virus

<400> 1

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His	His	Asn	Met	Val	Tyr	Ala	Thr	Ser	Arg	Ser	Ala	Gly	Leu	Arg	
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Arg	Asp	Val	Leu	Lys	Glu	Met	Lys	Ala	Lys	Ala	Ser	Thr	Val	Lys	Ala
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Lys	Leu	Leu	Ser	Val	Glu	Glu	Ala	Cys	Lys	Leu	Thr	Pro	Pro	His	Ser
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Asp	Thr	Val	Thr	Pro	Ile	Asp	Thr	Thr	Ile	Met	Ala	Lys	Asn	Glu	Val
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Phe	Cys	Val	Gln	Pro	Glu	Lys	Gly	Gly	Arg	Lys	Pro	Ala	Arg	Leu	Ile
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Val	Phe	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr
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Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu
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Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
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Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
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Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu
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Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly
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His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile
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Phe	Met	Lys	Leu	Gly	Ala	Leu	Thr	Gly	Thr	Tyr	Ile	Tyr	Asn	His	Leu
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Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu	Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu
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625 630 635 640
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645 650 655
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690 695 700
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740 745 750
Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys
755 760 765
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770 775 780
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785 790 795 800
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820 825 830
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835 840 845
Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr
850 855 860
Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser
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930 935 940
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995 1000 1005
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## SEQUENCE LISTING

## GENERAL INFORMATION

- (i) APPLICANT: ISTITUTO DI RICERCHE DI BIOLOGIA  
MOLECOLARE P. ANGELETTI S.p.A.
- 5 (ii) TITLE OF INVENTION: METHOD FOR REPRODUCING  
IN VITRO THE RNA-DEPENDENT RNA POLYMERASE  
AND TERMINAL NUCLEOTIDYL TRANSFERASE  
ACTIVITIES ENCODED BY HEPATITIS C VIRUS  
(HCV)
- 10 (iii) NUMBER OF SEQUENCES: 14
- (iv) CORRESPONDENCE ADDRESS:  
(A)ADDRESSEE: Societa Italiana Brevetti  
(B)STREET: Piazza di Pietra, 39  
(C)CITY: Rome
- 15 (D)COUNTRY: Italy  
(E)POSTAL CODE: 1-00186
- (v) COMPUTER READABLE FORM:  
(A)MEDIUM TYPE: Floppy disk 3.5" 1.44  
MBYTES
- 20 (B)COMPUTER: IBM PC compatible  
(C)OPERATING SYSTEM: PC-DOS/MS-DOS Rev.6.22  
(D)SOFTWARE: Microsoft Word 6.0
- (viii) ATTORNEY INFORMATION  
(A)NAME: DI CERBO, Mario (Dr.)
- 25 (C)REFERENCE: RM/X88530/PCT-DC
- (ix) TELECOMMUNICATION INFORMATION  
(A)TELEPHONE: 06/6785941  
(B)TELEFAX: 06/6794692  
(C)TELEX: 612287 ROPAT
- 30 (1) INFORMATION FOR SEQ ID NO: 1:
- (i) SEQUENCE CHARACTERISTICS  
(A)LENGTH: 591 amino acids  
(B)TYPE: amino acid
- 35 (C)STRANDEDNESS: single  
(D)TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein

SUBSTITUTE SHEET (RULE 26)

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- (iii) HYPOTHETICAL: No  
 (iv) ANTISENSE: No  
 (v) FRAGMENT TYPE: C-terminal fragment  
 (vi) ORIGINAL SOURCE:  
 5 (A) ORGANISM: Hepatitis C Virus  
 (C) ISOLATE : BK  
 (vii) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4)  
 described by Tomei et al. 1993  
 (ix) FEATURE:  
 10 (A) NAME: NSSB Non-structural polyprotein  
 (C) IDENTIFICATION METHOD: Experimentally  
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
- |    |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    | Ser | Met | Ser | Tyr | Thr | Trp | Thr | Gly | Ala | Leu | Ile | Thr | Pro | Cys | Ala | Ala | 1   | 5   | 10  | 15  |
| 15 | Glu | Glu | Ser | Lys | Leu | Pro | Ile | Asn | Ala | Leu | Ser | Asn | Ser | Leu | Leu | Arg | 20  | 25  | 30  |     |
|    | His | His | Asn | Met | Val | Tyr | Ala | Thr | Thr | Ser | Arg | Ser | Ala | Gly | Leu | Arg | 35  | 40  | 45  |     |
| 20 | Gln | Lys | Lys | Val | Thr | Phe | Asp | Arg | Leu | Gln | Val | Leu | Asp | Asp | His | Tyr | 50  | 55  | 60  |     |
|    | Arg | Asp | Val | Leu | Lys | Glu | Met | Lys | Ala | Lys | Ala | Ser | Thr | Val | Lys | Ala | 65  | 70  | 75  | 80  |
|    | Lys | Leu | Leu | Ser | Val | Glu | Glu | Ala | Cys | Lys | Leu | Thr | Pro | Pro | His | Ser | 85  | 90  | 95  |     |
| 25 | Ala | Lys | Ser | Lys | Phe | Gly | Tyr | Gly | Ala | Lys | Asp | Val | Arg | Asn | Leu | Ser | 100 | 105 | 110 |     |
|    | Ser | Lys | Ala | Val | Asn | His | Ile | His | Ser | Val | Trp | Lys | Asp | Leu | Leu | Glu | 115 | 120 | 125 |     |
| 30 | Asp | Thr | Val | Thr | Pro | Ile | Asp | Thr | Thr | Ile | Met | Ala | Lys | Asn | Glu | Val | 130 | 135 | 140 |     |
|    | Phe | Cys | Val | Gln | Pro | Glu | Lys | Gly | Gly | Arg | Lys | Pro | Ala | Arg | Leu | Ile | 145 | 150 | 155 | 160 |
|    | Val | Phe | Pro | Asp | Leu | Gly | Val | Arg | Val | Cys | Glu | Lys | Met | Ala | Leu | Tyr | 165 | 170 | 175 |     |
| 35 | Asp | Val | Val | Ser | Thr | Leu | Pro | Gln | Val | Val | Met | Gly | Ser | Ser | Tyr | Gly | 180 | 185 | 190 |     |
|    | Phe | Gln | Tyr | Ser | Pro | Gly | Gln | Arg | Val | Glu | Phe | Leu | Val | Asn | Thr | Trp |     |     |     |     |

SUBSTITUTE SHEET (RULE 26)

	195	200	205
	Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe		
	210	215	220
5	Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr		
	225	230	235 240
	Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu		
	245	250	255
	Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln		
10	260	265	270
	Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser		
	275	280	285
	Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg		
	290	295	300
15	Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu		
	305	310	315 320
	Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu		
	325	330	335
	Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp		
20	340	345	350
	Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser		
	355	360	365
	Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu		
	370	375	380
25	Thr Arg Asp Pro Thr Thr Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala		
	385	390	395 400
	Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala		
	405	410	415
	Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile		
30	420	425	430
	Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr		
	435	440	445
	Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu		
	450	455	460
35	Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser Tyr Ser Pro Gly		
	465	470	475 480
	Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro		

15

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 2201 amino acids

(B) TYPE: amino acid

20

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: polypeptide

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

25.

(v) FRAGMENT TYPE: C-terminal fragment

(vii) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4) described by Tomei et al. 1993

(ix) FEATURE:

30

(A) NAME: NS2-NS5B Nonstructural Protein Precursor

(C) IDENTIFICATION METHOD: Experimentally

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Val Gly  
1 5 10 15

35

Leu Val Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Phe Leu Ala Arg  
20 25 30

Leu Ile Trp Trp Leu Gln Tyr Phe Thr Thr Arg Ala Glu Ala Asp Leu

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	35	40	45
	His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile		
	50	55	60
	Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr		
5	65	70	75
	Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly		
	85	90	95
	Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala		
	100	105	110
10	Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala		
	115	120	125
	Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu		
	130	135	140
	Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val		
15	145	150	155
	Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr		
	165	170	175
	Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro		
	180	185	190
20	Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser		
	195	200	205
	Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser		
	210	215	220
	Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly		
25	225	230	235
	Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala		
	245	250	255
	Thr Gln Ser Phe Leu Ala Thr Cys Val Asn Gly Val Cys Trp Thr Val		
	260	265	270
30	Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Ala Pro Lys Gly Pro Ile		
	275	280	285
	Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu Val Gly Trp Pro Lys		
	290	295	300
	Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp		
35	305	310	315
	Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg		
	325	330	335

SUBSTITUTE SHEET (RULE 26)

Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro Val Ser Tyr Leu  
 340 345 350

5 Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val  
 355 360 365

Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val  
 370 375 380

Asp Phe Val Pro Val Glu Ser Met Glu Thr Thr Met Arg Ser Pro Val  
 385 390 395 400

10 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val  
 405 410 415

Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro  
 420 425 430

15 Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu Val Leu Asn Pro Ser  
 435 440 445

Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly  
 450 455 460

Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala  
 465 470 475 480

20 Pro Val Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly Cys  
 485 490 495

Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser Thr  
 500 505 510

25 Asp Ser Thr Thr Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala Glu  
 515 520 525

Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro Gly  
 530 535 540

Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn  
 545 550 555 560

30 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile  
 565 570 575

Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp  
 580 585 590

35 Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr  
 595 600 605

Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val  
 610 615 620

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	Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp	
	625	630 635 640
5	Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser	
	645	650 655
	Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Thr Val Pro Gln Asp Ala	
	660	665 670
	Val Ser Arg Ser Gln Arg Arg Gly Arg Thr Gly Arg Gly Arg Arg Gly	
	675	680 685
10	Ile Tyr Arg Phe Val Thr Pro Gly Glu Arg Pro Ser Gly Met Phe Asp	
	690	695 700
	Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu	
	705	710 715 720
	Leu Thr Pro Ala Glu Thr Ser Val Arg Leu Arg Ala Tyr Leu Asn Thr	
15	725	730 735
	Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val	
	740	745 750
	Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys	
	755	760 765
20	Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val	
	770	775 780
	Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys	
	785	790 795 800
	Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu	
25	805	810 815
	Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile	
	820	825 830
	Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Val Thr	
	835	840 845
30	Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr	
	850	855 860
	Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser	
	865	870 875 880
	Gly Arg Pro Ala Ile Val Pro Asp Arg Glu Leu Leu Tyr Gln Glu Phe	
35	885	890 895
	Asp Glu Met Glu Glu Cys Ala Ser His Leu Pro Tyr Ile Glu Gln Gly	
	900	905 910

SUBSTITUTE SHEET (RULE 26)

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	Met	Gln	Leu	Ala	Glu	Gln	Phe	Lys	Gln	Lys	Ala	Leu	Gly	Leu	Leu	Gln
	915							920					925			
5	Thr	Ala	Thr	Lys	Gln	Ala	Glu	Ala	Ala	Ala	Pro	Val	Val	Glu	Ser	Lys
	930							935					940			
	Trp	Arg	Ala	Leu	Glu	Thr	Phe	Trp	Ala	Lys	His	Met	Trp	Asn	Phe	Ile
	945							950					955			960
	Ser	Gly	Ile	Gln	Tyr	Leu	Ala	Gly	Leu	Ser	Thr	Leu	Pro	Gly	Asn	Pro
								965					970			975
10	Ala	Ile	Ala	Ser	Leu	Met	Ala	Phe	Thr	Ala	Ser	Ile	Thr	Ser	Pro	Leu
								980					985			990
	Thr	Thr	Gln	Ser	Thr	Leu	Leu	Phe	Asn	Ile	Leu	Gly	Gly	Trp	Val	Ala
								995					1000			1005
	Ala	Gln	Leu	Ala	Pro	Pro	Ser	Ala	Ala	Ser	Ala	Phe	Val	Gly	Ala	Gly
15								1010					1015			1020
	Ile	Ala	Gly	Ala	Ala	Val	Gly	Ser	Ile	Gly	Leu	Gly	Lys	Val	Leu	Val
	1025							1030					1035			1040
	Asp	Ile	Leu	Ala	Gly	Tyr	Gly	Ala	Gly	Val	Ala	Gly	Ala	Leu	Val	Ala
								1045					1050			1055
20	Phe	Lys	Val	Met	Ser	Gly	Glu	Met	Pro	Ser	Thr	Glu	Asp	Leu	Val	Asn
								1060					1065			1070
	Leu	Leu	Pro	Ala	Ile	Leu	Ser	Pro	Gly	Ala	Leu	Val	Val	Gly	Val	Val
								1075					1080			1085
	Cys	Ala	Ala	Ile	Leu	Arg	Arg	His	Val	Gly	Pro	Gly	Glu	Gly	Ala	Val
25								1090					1095			1100
	Gln	Trp	Met	Asn	Arg	Leu	Ile	Ala	Phe	Ala	Ser	Arg	Gly	Asn	His	Val
	1105							1110					1115			1120
	Ser	Pro	Thr	His	Tyr	Val	Pro	Glu	Ser	Asp	Ala	Ala	Ala	Arg	Val	Thr
								1125					1130			1135
30	Gln	Ile	Leu	Ser	Ser	Leu	Thr	Ile	Thr	Gln	Leu	Leu	Lys	Arg	Leu	His
								1140					1145			1150
	Gln	Trp	Ile	Asn	Glu	Asp	Cys	Ser	Thr	Pro	Cys	Ser	Gly	Ser	Trp	Leu
								1155					1160			1165
	Arg	Asp	Val	Trp	Asp	Trp	Ile	Cys	Thr	Val	Leu	Thr	Asp	Phe	Lys	Thr
35								1170					1175			1180
	Trp	Leu	Gln	Ser	Lys	Leu	Leu	Pro	Gln	Leu	Pro	Gly	Val	Pro	Phe	Phe
	1185							1190					1195			1200

SUBSTITUTE SHEET (RULE 26)



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Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile Met  
1205 1210 1215

Gln Thr Thr Cys Pro Cys Gly Ala Gln Ile Thr Gly His Val Lys Asn  
5 1220 1225 1230

Gly Ser Met Arg Ile Val Gly Pro Lys Thr Cys Ser Asn Thr Trp His  
1235 1240 1245

Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro Ser  
1250 1255 1260

10 Pro Ala Pro Asn Tyr Ser Arg Ala Leu Trp Arg Val Ala Ala Glu Glu  
1265 1270 1275 1280

Tyr Val Glu Val Thr Arg Val Gly Asp Phe His Tyr Val Thr Gly Met  
1285 1290 1295

Thr Thr Asp Asn Val Lys Cys Pro Cys Gln Val Pro Ala Pro Glu Phe  
15 1300 1305 1310

Phe Ser Glu Val Asp Gly Val Arg Leu His Arg Tyr Ala Pro Ala Cys  
1315 1320 1325

Arg Pro Leu Leu Arg Glu Glu Val Thr Phe Gln Val Gly Leu Asn Gln  
1330 1335 1340

20 Tyr Leu Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val Ala  
1345 1350 1355 1360

Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu Thr  
1365 1370 1375

Ala Lys Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Leu Ala Ser Ser  
25 1380 1385 1390

Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr Thr  
1395 1400 1405

His His Val Ser Pro Asp Ala Asp Leu Ile Glu Ala Asn Leu Leu Trp  
1410 1415 1420

30 Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn Lys  
1425 1430 1435 1440

Val Val Val Leu Asp Ser Phe Asp Pro Leu Arg Ala Glu Glu Asp Glu  
1445 1450 1455

Arg Glu Val Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Lys Lys Phe  
35 1460 1465 1470

Pro Ala Ala Met Pro Ile Trp Ala Arg Pro Asp Tyr Asn Pro Pro Leu  
1475 1480 1485

SUBSTITUTE SHEET (RULE 26)

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	Leu Glu Ser Trp Lys Asp Pro Asp Tyr Val Pro Pro Val Val His Gly
	1490 1495 1500
5	Cys Pro Leu Pro Pro Ile Lys Ala Pro Pro Ile Pro Pro Pro Arg Arg
	1505 1510 1515 1520
	Lys Arg Thr Val Val Leu Thr Glu Ser Ser Val Ser Ser Ala Leu Ala
	1525 1530 1535
	Glu Leu Ala Thr Lys Thr Phe Gly Ser Ser Glu Ser Ser Ala Val Asp
	1540 1545 1550
10	Ser Gly Thr Ala Thr Ala Leu Pro Asp Gln Ala Ser Asp Asp Gly Asp
	1555 1560 1565
	Lys Gly Ser Asp Val Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu Gly
	1570 1575 1580
	Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val Ser
15	1585 1590 1595 1600
	Glu Glu Ala Ser Glu Asp Val Val Cys Cys Ser Met Ser Tyr Thr Trp
	1605 1610 1615
	Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro
	1620 1625 1630
20	Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Met Val Tyr
	1635 1640 1645
	Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg Gln Lys Lys Val Thr Phe
	1650 1655 1660
	Asp Arg Leu Gln Val Leu Asp Asp His Tyr Arg Asp Val Leu Lys Glu
25	1665 1670 1675 1680
	Met Lys Ala Lys Ala Ser Thr Val Lys Ala Lys Leu Leu Ser Val Glu
	1685 1690 1695
	Glu Ala Cys Lys Leu Thr Pro Pro His Ser Ala Lys Ser Lys Phe Gly
	1700 1705 1710
30	Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser Ser Lys Ala Val Asn His
	1715 1720 1725
	Ile His Ser Val Trp Lys Asp Leu Leu Glu Asp Thr Val Thr Pro Ile
	1730 1735 1740
	Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln Pro Glu
35	1745 1750 1755 1760
	Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp Leu Gly
	1765 1770 1775

SUBSTITUTE SHEET (RULE 26)

Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Ser Thr Leu  
 1780 1785 1790

5 Pro Gln Val Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser Pro Gly  
 1795 1800 1805

Gln Arg Val Glu Phe Leu Val Asn Thr Trp Lys Ser Lys Lys Asn Pro  
 1810 1815 1820

Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val Thr Glu  
 1825 1830 1835 1840

10 Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Gln Cys Cys Asp Leu Ala  
 1845 1850 1855

Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu Thr Glu Arg Leu Tyr Ile  
 1860 1865 1870

15 Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg  
 1875 1880 1885

Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr  
 1890 1895 1900

Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp  
 1905 1910 1915 1920

20 Cys Thr Met Leu Val Asn Gly Asp Asp Leu Val Val Ile Cys Glu Ser  
 1925 1930 1935

Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg Val Phe Thr Glu Ala  
 1940 1945 1950

25 Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr  
 1955 1960 1965

Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val Ala His  
 1970 1975 1980

Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro Thr Thr  
 1985 1990 1995 2000

30 Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro Val Asn  
 2005 2010 2015

Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala Pro Thr Leu Trp Ala Arg  
 2020 2025 2030

35 Met Ile Leu Met Thr His Phe Phe Ser Ile Leu Leu Ala Gln Glu Gln  
 2035 2040 2045

Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr Gly Ala Cys Tyr Ser Ile  
 2050 2055 2060

SUBSTITUTE SHEET (RULE 26)

5	Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg Val Ala	2085	2090	2095
	Ser Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Val Trp Arg His	2100	2105	2110
	Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ser Gln Gly Gly Arg Ala	2115	2120	2125
0	Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Lys Thr Lys Leu	2130	2135	2140
	Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg Leu Asp Leu Ser Gly Trp	2145	2150	2155
	Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Leu Ser Arg	2165	2170	2175
	Ala Arg Pro Arg Trp Phe Met Leu Cys Leu Leu Leu Leu Ser Val Gly	2180	2185	2190
	Val Gly Ile Tyr Leu Leu Pro Asn Arg	2195	2200	

(3) INFORMATION FOR SEQ ID NO: 3

- (i) SEQUENCE CHARACTERISTICS
  - (A) LENGTH: 26 nucleotides
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: synthetic DNA
- (iii) HYPOTHETICAL: No
- (iv) ANTISENSE: No
- (vii) IMMEDIATE SOURCE: oligonucleotide synthesizer
- (ix) FEATURE:
  - (A) NAME: oligo a
  - (C) IDENTIFICATION METHOD: Polyacrylamide gel
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3

GCCGAGATGC CATCTTCAAA CAGTTC

26

## (4) INFORMATION FOR SEQ ID NO: 4

## (i) SEQUENCE CHARACTERISTICS

- 5 (A) LENGTH: 24 nucleotides  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: synthetic DNA

## 10 (iii) HYPOTHETICAL: No

## (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

## (ix) FEATURE:

## 15 (A) NAME: oligo b

(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4

20 GTGTACAACA AGGTCCATAT CACC

24

## (5) INFORMATION FOR SEQ ID NO: 5

## (i) SEQUENCE CHARACTERISTICS

- 25 (A) LENGTH: 24 nucleotides  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: single  
(D) TOPOLOGY: linear

## (ii) MOLECULE TYPE: synthetic DNA

## (iii) HYPOTHETICAL: No

## 30 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

## (ix) FEATURE:

## 35 (A) NAME: oligo c

(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

## (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5

GGTCTTTCTG AACGGGATAT AAAC

24

(6) INFORMATION FOR SEQ ID NO: 6:

5 (i) SEQUENCE CHARACTERISTICS  
(A)LENGTH: 31 nucleotides  
(B)TYPE: nucleic acid  
(C)STRANDEDNESS: single  
(D)TOPOLOGY: linear

10 (ii) MOLECULE TYPE: synthetic DNA  
(iii) HYPOTHETICAL: No  
(iv) ANTISENSE: No  
(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

15 (ix) FEATURE:  
(A)NAME: 5'-5B  
(C)IDENTIFICATION METHOD: Polyacrylamide  
gel

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6

AAGGATCCAT GTCAATGTCC TACACATGGA C 31

(7) INFORMATION FOR SEQ ID NO: 7:

25 (i) SEQUENCE CHARACTERISTICS  
(A)LENGTH: 36 nucleotides  
(B)TYPE: nucleic acid  
(C)STRANDEDNESS: single  
(D)TOPOLOGY: linear

30 (ii) MOLECULE TYPE: synthetic DNA  
(iii) HYPOTHETICAL: No  
(iv) ANTISENSE: Yes  
(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

35 (ix) FEATURE:  
(A)NAME: 3'-5B  
(C)IDENTIFICATION METHOD: Polyacrylamide  
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7

AATATTCGAA TTCATCGGTT GGGGAGCAGG TAGATG

36

5 (8) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS  
(A) LENGTH: 22 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

(ix) FEATURE:

(A) NAME: Dpr1

(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8

TGGCTGGCAA GGCACACAGG CT

22

25 (9) INFORMATION FOR SEQ ID NO: 9

(i) SEQUENCE CHARACTERISTICS  
(A) LENGTH: 20 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

35 (ix) FEATURE:

(A) NAME: Dpr2

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(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9

5 AGGCAGGGTA GATCTATGTC 20

(10) INFORMATION FOR SEQ ID NO: 10

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 20 nucleotides

10 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

15 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

(ix) FEATURE:

(A) NAME: NS5B-5' (1)

20 (C) IDENTIFICATION METHOD: Polyacrylamide  
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10

TCAATGTCCT ACACATGGAC 20

25

(11) INFORMATION FOR SEQ ID NO: 11

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 38 nucleotides

(B) TYPE: nucleic acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

35 (vii) IMMEDIATE SOURCE: oligonucleotide  
synthesizer

(ix) FEATURE:

SUBSTITUTE SHEET (RULE 26)



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(A) NAME: HCVA-13

(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11

5

GATCTCTAGA TCATCGGTTG GGGGAGGAGG TAGATGCC

38

(12) INFORMATION FOR SEQ ID NO: 12

(i) SEQUENCE CHARACTERISTICS

10

(A) LENGTH: 399 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA

15

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Rattus Norvegicus

(B) STRAIN : Sprague-Dawley

20

(vii) IMMEDIATE SOURCE: pT7-7 (DCoH)

(ix) FEATURE:

(A) NAME: D-RNA

(C) IDENTIFICATION METHOD: Polyacrylamide  
gel

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12

GGGAGACCAC AACGGUUUCC CUCUAGAAAU AAUUUUGUUU AACUUUAAGA AGGAGAUAVA 60

CAUAUGGCUA GAAUUCGCGC CCUGGCUGGC AAGGCACACA GGCUGAGUGC UGAGGAACGG 120

GACCAGCUGC UGCCAAACCU GCGGGCCGUG GGGUGGAUG AACUGGAAGG CCGAGAUGCC 180

30 AUCUCAAAC AGUCCAUUU UAAAGACUUC AACAGGGCUU UUGGCUUCAU GACAAGAGUC 240

GCCCUGCAGG CUGAAAAGCU GGACCACCAU CCCGAGUGGU UUAACGUGUA CAACAAGGUC 300

CAUAUCACCU UGAGCACCCA CGAUGUGCC GGUCUUUCUG AACGGGAUAV AAACCUGGCC 360

AGCUUCAUCG AACAAGUUGC CGUGUCUAVG ACAUAGAUC 399

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(13) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 20 nucleotides

(B) TYPE: nucleic acid

5 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

10 (vii) IMMEDIATE SOURCE: oligonucleotide synthesizer

(ix) FEATURE:

(A) NAME: NS5B-up

(C) IDENTIFICATION METHOD: Polyacrylamide gel

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13

TGTC AATGTC CTACACATGG

20

(14) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS

20 (A) LENGTH: 38 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

25 (iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

(vii) IMMEDIATE SOURCE: oligonucleotide synthesizer

(ix) FEATURE:

(A) NAME: 3'-5B

30 (C) IDENTIFICATION METHOD: Polyacrylamide gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14

AATATTCGAA TTCATCGGTT GGGGAGCAGG TAGATG

36